RESEARCH ARTICLE

Epidemiology of Leukemia and Multiple Myeloma in Golestan, Iran

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Abstract

Background: The aim of this paper was to present the incidence rates of leukemia and multiple myeloma (MM) in Golestan province located in northeastern Iran during 2004-2009. Materials and Methods: This was a descriptive cross-sectional study. Data on newly diagnosed (incident) leukemia and MM cases were obtained from collected from Golestan population-based cancer registry. Data was entered into CanReg-4 software. Age standardized incidence rates (ASR) (per 100000 person-years) for leukemia and MM were calculated. Data on Golestan population was obtained from the data of Iranian national census in 2006. Results: Totally, 11036 new cancer cases were registered in GPRC from 2004-2009. Leukemia and MM accounted for 693 and 124 of cases, respectively. The mean age in patients with leukemia and MM was 43.8 and 62.4 years, respectively. The ASRs for leukemia among men and women were 10.4 and 7.8, respectively (p<0.001). The ASRs for MM were 2.1 and 2 in men and women, respectively (p=0.93). The rate of leukemia was significantly higher in rural areas (p=0.02) whereas the incidence of MM was higher in urban areas (p<0.001). Conclusions: Our results showed a high incidence rate of leukemia in Golestan province of Iran. The incidence of leukemia was significantly higher in males and residents of rural areas. High exposure to pesticides and other agricultural related products may be a possible explanation for epidemiological pattern of leukemia in this area. Determining and controlling important risk factors, especially environmental factors, of leukemia may lead to decrease in its burden in Golestan province of Iran.

Keywords: Leukemia - multiple myeloma - epidemiology - Golestan - Iran

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Introduction

Cancer is one of the leading causes of death in the world. It was estimated that 12 million new cases of cancer were occurred all over the world. Cancers accounted for 7.6 million deaths (13% of all deaths) in 2008. According to Globocan 2008, the age-standardized incidence rates (ASR) of all cancers were 202.8 and 164.4 per 100000 person-year among male and female, respectively. Leukemias were reported as one of the 9th and 10th common cancers in men and women, respectively (Ferlay et al., 2010).

Leukemias are a hetrogenous group of hematopoietic malignancies that included four major subtypes of leukemias described by most cancer registries include Acute Lymphoblastic Leukemia (ALL), Acute Myeloid Leukemia (AML), Chronic Lymphoblastic Leukemia (CLL), and Chronic Myeloid Leukemia (CML) (Xie et al., 2003). Multiple Myeloma (MM) is a malignancy of B-cells that is characterized by aberrant expansion and accumulation of malignant plasma cells in the bone marrow (Laubach et al., 2009).

As stated in Globocan 2008, the ASRs of leukemia in men and women were 5.8 and 4.3 per 100000 person-year, respectively, all over the world. In more developed countries the rates were 9.1 and 5.9 per 100000 person-year for male and female, respectively. These rates in less developed regions were 4.0 and 3.3 per 100000 person-year in men and women, respectively. In Iran, the ASRs of leukemia were 7.7 and 4.0 per 100000 person-year among male and female, respectively. Epidemiology of MM is similar to the leukemias. The ASRs of MM are higher in developed countries (male=3.3, female=2.2 per 100000 person-year) than less developed areas (male= 0.7, female=0.8 per 100000 person- year). Risk factors for leukemia are previous chemotherapy, genetic disorders caused by abnormal chromosomes, human T cell leukemia virus, myelodysplastic syndrome (Rhomberg et al., 2011). Age and race are considered as risk factors for multiple myeloma. Exposure to radiation and occupational

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exposures to high levels of benzene or formaldehyde are considered as risk factors for both multiple myeloma and leukemia (Romanenko et al., 2008; Yiin et al., 2009; Rhomberg et al., 2011).

Monitoring the trend in cancer incidence is one of the most important functions of cancer surveillance system. Changes in the incidence of cancer in population can provide important information regarding potential changes in risk factors. It can help us approach more strategic to control cancers. Golestan Population-based Cancer Registry (GPCR) was established to achieve this goal in a high risk area for upper gastrointestinal cancers, so called as Golestan province of Iran. GPCR has been approved as a voting member of the International Association of Cancer Registries (IACR) and is now going on as a qualified cancer registry (Roshandel et al., 2012). The aim of this paper is to present the incidence rates of leukemia and multiple myeloma in GPCR during 2004-2009.

Materials and Methods

This was a descriptive cross-sectional study. GPCR registered only primary cancers while additional tumors that result from the invasion or metastasis of cancers to other organs were not considered. Malignant tumors of all organs were registered based on the IACR standards. Data on newly diagnosed (incident) leukemia and MM cases were collected from all public and private diagnostic and therapeutic centers (hospitals, pathology/laboratory centers, imaging centers and some of the specialist physician's private offices) of the whole province. GPCR also had close collaboration with some of medical centers and regional registries outside the province to minimize loss of the data and consequent underestimation. Incidence data discussed in this paper are based on cases of primary cancers which were first diagnosed among Golestan residents from 2004-2009.

Two kinds of questionnaires, the first for outpatient and the second for inpatient cases, were used for data collection. Items collected in GPCR consisted of the patient's demographic particulars, anatomical site of the cancer, histology of tumor, method of diagnosis, date of diagnosis, method of treatment and outcome (date of death in case the patient has died). In some centers, data was collected passively ie, notifications of diagnosed cases were sent to the GPCR office on a routine, continuing basis. Thirty four health professionals underwent specific training for data abstraction in these centers. Data collection in other centers was active, the registry staff regularly visited them and collected information on newly diagnosed cancer cases. Ten percent of questionnaires were checked and compared with original documents in the source centers to verify accuracy and completeness of the abstraction process.

For classification of the lesions the third edition of International Classification of Diseases for Oncology (ICD-O-3) (Fritz et al., 2000) coding system was used; it applied the rules, nomenclature and codes (morphology, topography, and behavior) of malignant disease. IARC multiple primary rules (International Agency for Reseach on Cancer, 2004) were used for patients with malignant tumors in more than one site. Data was entered into CanReg-4 software (Parkin and Ferlay, 2001), created and published by the IACR. Finally, number of cases by sex, age and primary site as well as age standardized incidence rates (ASR) (per 100000 person-years) for cancers were calculated.

We needed the data of Golestan population to calculate incidence rates. It was obtained from the Iranian national census. The Iranian national census is held every 5 years by the Iranian statistical center. The most recent census was held in 2011. Regarding the period of our study (2004-2009), we used the data of Iranian national census in 2006.

Staff of the registry were educated and asked to consider confidentiality in all stages of registry process including collection on notifications, transmission of information, access to and storage of data, use and release of data and record linkage. Confidentiality measures were used to ensure the preservation of anonymity of cancer cases, the best quality of registry data and the best possible usage of the data. Ethical issues of this project were approved by the ethical committee of Golestan University of Medical Sciences.

Results

Totally, 11036 new cancer cases were registered in GPRC from 2004-2009. Leukemia and multiple myeloma accounted for 693 and 124 of incident cases, respectively. The mean (SD) of age at diagnosis in patients with leukemia and multiple myeloma were 43.8 (24.7) and 62.4 (12.5) years, respectively. Table 1 shows the characteristics of patients with leukemia and multiple myeloma in Golestan province.

The age-standard incidence rates for leukemia among men and women were 10.4 and 7.8 per 100,000 person-year, respectively (p value<0.001). The ASRs for multiple myeloma were 2.1 and 2 per 100000person-year in men and women, respectively (p value=0.93).

Table 2 presents number, crude rates and Age-Standardized Rates (ASRs) of leukemia and multiple myeloma among men and women in Golestan province. Age-specific incidence rates for leukemia and multiple myeloma in males and females have been shown in Figure 1.

The ASR of leukemia in urban and rural areas were 8.6 and 9.7 per 100000 person-years, respectively (p value=0.02). The ASRs of multiple myeloma were 2.7

Table 1. Characteristics of Patients with Leukemia and Multiple Myeloma in Golestan Province, Iran, 2004-2009

Variable		Leukemia No.	%	Multiple Myeloma No.	%
Gender	Male	408	58.0	63	50.8
	Female	291	42.0	61	49.2
Place of residence	Urban	310	44.7	84	67.7
	Rural	383	55.3	40	32.3
Method of diagnosis	Cytology	184	26.6	0	0
	Histology	509	73.4	124	100

Table 2. Number of Patients, Crude Rate* and Age Standardized Incidence Rate (ASR)* of Leukemia and Multiple Myeloma in Golestan Province, Iran, 2004-2009

		Male			Female		
		No.	Crude rate	ASR	No.	Crude rate	ASR
Urban	Multiple Myeloma	40	1.6	2.5	44	1.8	3.0
	Lymphoid Leukemia	95	3.9	5.2	42	1.8	2.5
	Myeloid Leukemia	47	1.9	2.6	32	1.3	1.9
	Leukemia unspec.	43	1.8	2.4	51	2.1	2.7
Rural	Multiple Myeloma	23	0.9	1.7	17	0.7	1.1
	Lymphoid Leukemia	91	3.6	4.4	55	2.2	2.6
	Myeloid Leukemia	46	1.8	2.4	54	2.2	2.8
	Leukemia unspec.	80	3.2	4.1	57	2.3	3.0
Total	Multiple Myeloma	63	1.3	2.1	61	1.3	2.0
	Lymphoid Leukemia	186	3.7	4.7	97	2.0	2.6
	Myeloid Leukemia	93	1.9	2.5	86	1.8	2.3
	Leukemia unspec.	123	2.5	3.2	108	2.2	2.9

*Per 100000 person-years

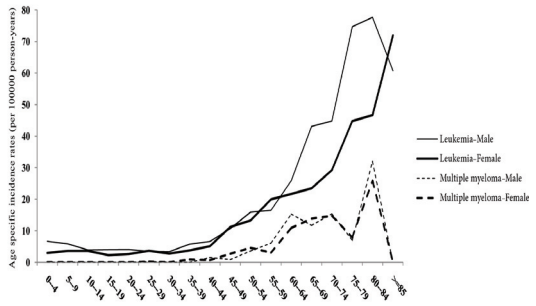

Figure 1. Age Specific Incidence Rates of Leukemia and Multiple Myeloma in Golestan Province of Iran, 2004-2009

and 1.5 per 100000 person-years in urban and rural areas, respectively (p value<0.001). Male patients living in urban area had lower rate of leukemia than those living in rural areas (p value=0.19). This difference was significant in female patients (p value=0.04). The incidence rate of multiple myeloma was significantly higher in urban males than rural ones (p value=0.02). Similar significant difference was seen in female patients (p value<0.001).

Discussion

In this population-based study conducted in Golestan province, northeast of Iran, we found that the ASR of leukemia in men and women in Golestan province were 10.4 and 7.8 per 100000 person-years, respectively. These rates were higher than those reported for Iran (7.7 and 4.0 per 100000 person-years for men and women) and the world (5.8 and 4.3 per 100000 person-years for men and women) (Ferlay et al., 2010). Our results also showed higher rate of leukemia in Golestan province than neighboring countries including Arab world (Salim et al., 2009; 2010). Our findings indicated that the ASR of multiple myeloma among males and females were 2.1 and 1 per 100000 person-years, respectively. The ASRs of multiple myeloma in Iran were 1.8 and 1 per 100000 person-years for male and females, respectively (Ferlay et al., 2010). Regarding the world population, the rates were 1.7 and 1.2 per 100000 person-years for males, respectively (Ferlay et al., 2010). So, the incidence rates of leukemia in Golestan province of Iran were relatively higher than those reported for Iran as well as the world. Further investigations are warranted to identify risk factors and determinants of leukemia in this area.

Our study showed that incidence rate of leukemia was significantly higher in males than females. The sex distribution pattern of leukemia in Golestan province was in line with those observed in other studies (Xie et al., 2003; Thygesen et al., 2009; Novak et al., 2012). It may be proposed that male gender is at higher risk of leukemia due to genetic predisposition or exposure to environmental factors.

The incidence rate of leukemia was significantly higher in rural areas than urban areas. Because of the variety of risk factors involved in etiology of leukemia, it is difficult to identify the reasons for the high incidence rate of leukemia in Golestan province, particularly in rural areas. Recent studies reported increased risk of leukemia among farmers (Brown et al., 1990; Turner et al., 2011). Golestan province, located at southeast of Caspian Sea, is one of the most important poles of Iran's farming and agricultural products. Consequently, high incidence of leukemia in rural parts of this area may be attributed to high exposure to potential hazardous substances including pesticide, grain dust, zoonotic viruses and microbes among those working routinely in farms (Brown et al., 1990).

The incidence rate of multiple myeloma was significantly higher among people living in urban areas than those from rural areas. Residents of urban areas may expose to some carcinogenic factors especially those related to the development of multiple myeloma. Previous studies suggested that exposure to engine exhaust, asbestos and benzene may increase the risk of multiple myeloma (Baris et al., 2004). Further studies are warranted to investigate the environmental risk factors of multiple myeloma in Golestan province.

In conclusion, we found a high incidence rate of leukemia in Golestan province of Iran. Our results also showed that the incidence of leukemia was significantly higher in male gender and residents of rural area. High exposure to pesticides and other agricultural related products may be a possible explanation for epidemiological pattern of leukemia in this area. Determining and controlling important risk factors, especially environmental factors, of leukemia may lead to decrease its burden in Golestan province of Iran.

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